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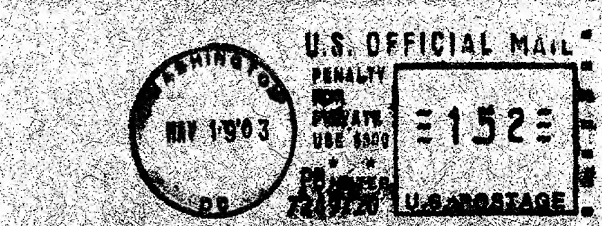

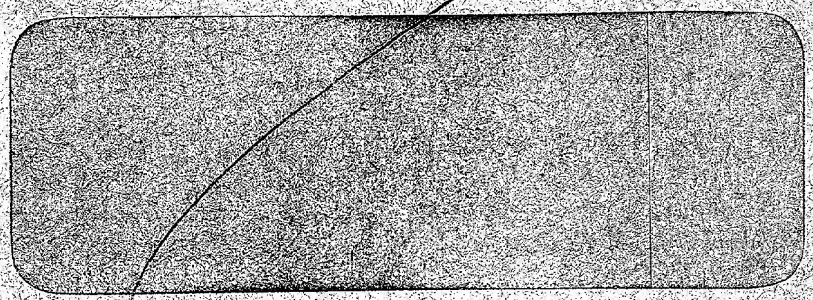

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,821	05/26/2000	GUY A. ROULEAU	2055MC/48747	1968

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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,821	ROULEAU ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9-11 and 13-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9-11 and 13-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *0303* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed March 13, 2003. Currently, claims 1-5, 9-11, 13-25 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn in view of the amendments to the claims and applicant's remarks.

Maintained Rejections

Priority

3. This application is a National Stage application of PCT/CA98/00884, filed September 18, 1998.

The application also claims priority to CANDA 2,216,057, filed September 19, 1997. The Canadian document does not teaches the sequence of (CAR)2(CAG)nCAA as essential to the hGT1 sequence. Moreover, the document does not appear to teach SEQ ID NO: 2, 5 or 6. Therefore, the instant claims do not receive benefit of the September 19, 1997 filing date.

New Matter

4. The amendment filed March 13, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added

material which is not supported by the original disclosure is as follows. Moreover, the amendments and comments provided in the response filed March 13, 2003 have been considered, but do not overcome the instant rejection.

At page 8, please amend lines 30-32 so that they now read: "The GTI sequence which includes an open-reading frame (ORF encoding 1755 amino acids without interruption) shows 85% homology to the mouse CDNA (Figs. 4A-4E) The sequence of GTI is from one large (5276 bp) Bam HI fragment and three Pst I fragments (672, 200 and 371 bps). This ORF is preceded by 490 bps. including a 470 bps intron"

Applicants have amended the specification to more clearly reflect the new matter problems contained in the sequence listing. Amending the specification can not overcome the new matter rejection with respect to the sequence listing. The response fails to point to any support for the 1755 amino acids and to the 470 bp intron. Therefore, each of these new limitations in the specification constitute new matter.

New Matter

5. The amendment filed December 1, 2001 and November 9, 2001 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows. Moreover, the amendments and comments provided in the response filed June 28, 2002 have been considered, but do not overcome the instant rejection.

Applicants have amended the Sequence listing to include new SEQ ID NO: 6-10. Applicants submit that the substitute sequence listing is provided to show the hGT1 amino acid sequence. "The pertinent portion of SEQ ID NO: 5 has been translated. Support for the translation of SEQ ID NO: 5 can be found in the specification at page 8, lines 30-32, describing the 5535 bp open reading frame. Support can also be found at page 8, lines 35 to page 9, line 2, describing the 490 bp intro preceding the ORF".

The specification the GT1 sequence includes a 5535 bp open-reading frame (ORF) of 5535 bps without interruption (page 8, lines 30-32). The specification teaches that the ORF is preceded by a 490 bp intron (including a consensus splice acceptor) and 19 bps of 5'UTR. The entire ORF may be coded for by a single exon (we are still missing the sequences coding for the last 12 amino acids (36 bp)) (page 9, lines 2-4).

While SEQ ID NO: 5 has been supported by the original disclosure, it appears as though the introduction of the protein sequence is not supported by the original disclosure. Based upon the text of the specification, it appears as though there are 490 bp plus 19 bps prior to the ORF, such that there are 509 bps prior to the translation start site. The amendment which has added the protein sequence appears to begin at nucleotide position 490. Therefore, there is neither a 490 bp intron preceding the ORF nor the 490 bp intron and 19 bps of the 5'UTR. Thus, insertion of a start site at position 490 does not appear to be supported by the original disclosure. The response filed June 28, 2002, page 5, attempts to explain the confusion and asserts that the translation of the nucleic acid in SEQ ID NO: 5 is not new matter since the translation was intrinsic to the sequence as originally filed. The response also states that a total of

490 bps including a 19 bps exon in the 5'UTR are upstream of the initiator codon. This also has not been supported since, the initiator occurs at 490, not with 490 prior to the start codon. Moreover, in the event that applicant finds support for the amendment, the specification requires clarification.

Furthermore, as provided in the brief description of the drawings, Figure 4 illustrates the nucleotide sequence of hGT1, wherein the upstream intron is in lowercase; human gene sequence (exon) is in upper case; and the transcription start site ATG in bold. The examiner does not see a bolded start site. The response filed June 28, 2002 submits that the oversight was a clerical error and submits a copy of the sequence provided by the inventor which was used to prepare the priority application, which shows the ATG at 490 is bold and the initator. While the examiner notes the provided sequence contains a bold ATG site. This however does not correct the application such that an ATG site in Figure 4 is in bold.

Moreover, SEQ ID NO: 5 contains numerous three letter 'tga' sites (stop codons) in the "coding sequence". This is indicative that this is not a coding region. SEQ ID NO: 6-10 are fragments from the start to stop sites, which are not supported by the original disclosure nor the original figures. The response filed June 28, 2002 agrees with the examiner that as presently translated, the amino acid sequence encoded by SEQ ID NO: 5 is truncated at amino acid 1755 such that numerous amino acids are missing from the C-terminus. Moreover, applicants argue that if a +1 frameshift is at 1755 of SEQ ID NO: 5, the ORF continues until 6022. However, this +1 frameshift is not supported by the instant specification.

Applicant's response states that "as of the filing of this response, the discrepancy in SEQ ID NO: 5 and the statement that 'TG1 includes 5535 bps open-reading frame (OFR) of 5535 bps with out interruption' is no understood". The examiner requests clarification of this discrepancy.

Moreover, the response has made no effort to explain SEQ ID NO: 7-10 and their support in the specification. SEQ ID NO: 7-10 appear to be the smaller fragments of the protein between the stop codons which are not supported by the instant specification.

Applicant is reminded that no new matter may be entered by amendment. Applicant is required to cancel the new matter in the reply to this Office Action.

Response to Arguments

The response asserts that the open reading frame of SEQ ID NO: 6 is supported by the specification as originally filed. Each of the points provided by the response are separately addressed.

1. Contrary to applicant's position, the specification states, on page 8-9, "This ORF is preceded by a 490 bps intron ... and 19 bps of 5' UTR." Therefore the specification does not state that the AUG initiator is at position 490, but rather suggests that the initiator is at position 490 + 19= 509.

2. The specification, prior to the instant amendment to the specification, fails to ever describe a "very long 1755 aa ORF." The specification alternatively teaches that the ORF is 5535 bps in length (page 8, lines 30-32). The nucleic acid of SEQ ID NO: 5 does contain a stretch of polyglutamines 14 glutamines in length.

3. While the sequence listing contains SEQ ID NO: 4 as an oligonucleotide, the specification does not teach using this oligonucleotide as a primer for amplification of the glutamine repeat. The specification appears to teach SE QI DNO: 3 and 11 for amplification (page 16, lines 16-17).

4. Figure 3 appears to provide an alignment between the human and the mouse. The bullet however does not provide any page number for the assertion. Therefore, this aspect has not been addressed.

5. The specification clearly teaches a 5535 base pair ORF without interruption. This would imply that there was no termination as the newly added 1755 ORF recitation in the specification.

The response further argues that "While admittedly the 3' end of SEQ ID NO:5 contains stop codons, it should be clear to the Examiner that until the first stop codon is reached in SEQ ID NO:5, a very significantly long open-reading frame is encoded thereby (1755 amino acids)." It is clear that the first stop codon is at 1755, however, this is not consistent with the specification. Therefore regardless as to whether it is "a very significantly long open reading frame" is not the standard for assessing new matter.

Applicant's response states that "as of the filing of this response, the discrepancy in SEQ ID NO: 5 and the statement that 'TG1 includes 5535 bps open-reading frame (OFR) of 5535 bps with out interruption' is no understood". The examiner requests clarification of this discrepancy. The response currently has not provided any

explanation for this discrepancy. The response merely amended the specification with out exaplaination.

Moreover, the specification has not been amended to cancel SEQ ID NO: 7-10 as suggested by the response. Thus for the reasons above and those already of record, the rejection is maintained.

New Matter

6. Claims 19-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "nucleic acid sequences comprising a sequence encoding the amino acid sequence as set forth in SEQ ID NO: 6" are included. However, the specification does not describe or discuses "nucleic acid sequences comprising a sequence encoding the amino acid sequence as set forth in SEQ ID NO: 6". The specification originally provided a single nucleotide sequence. By amendment, applicants are asserting that the protein translation is defined in the specification and supported. However, there is no indication that at the time of filing, the applicant's regarded their invention as nucleic acids encoding an amino acid sequence of SEQ ID NO: 6. The concept of "nucleic acid sequences comprising a sequence encoding the amino acid sequence as set forth in SEQ ID NO: 6" does not appear to be part of the originally filed invention. Therefore, "nucleic acid sequences comprising a

sequence encoding the amino acid sequence as set forth in SEQ ID NO: 6" constitutes new matter.

Moreover, the specification does not appear to teach vectors and cells comprising the SEQ ID NO: 2, 5 or the gene of Claim 1 or cells comprising the vectors. The concept of "vectors and "cells" do not appear to be part of the originally filed disclosure.

Applicant is required to cancel the new matter in the reply to this Office Action.

Response to Arguments

The response traverses the rejection. The response asserts that the open-reading frame or protein of SEQ ID NO: 5 is supported. This argument has been reviewed but is not convincing because the specification fails to teach that SEQ ID NO: 6 is the encoded protein of SE QID NO: 5. Based upon the confusion in start codon location and in stop codons addressed above, there is not support that SE QID NO: 6 is the protein encoded by SEQ ID NO: 5.

The response points to page 5-6 of the specification as supporting cells and vectors. The specification fails to describe or discuss cells and vectors comprising the nucleic acid. The transgenic animals referred to in the specification may be generated using alternative means, such as homologous recombination, rather than genetically engineering. Therefore, the specification fails describe or support vectors and cells.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 9-11, 13-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated human hGT1 gene comprising a transcribed polymorphic CAG repeat having the sequence (CAR)2(CAG)n(CAA) wherein R is A or G and n is from 7-12, wherein allelic variants of said CAG repeat are associated with a disorder and wherein n being equal to 11 is the most common allele of the hGT1 gene.

The specification describes a nucleic acid, SEQ ID NO: 5, which is 6022 nucleotides in length. The specification the GT1 sequence includes a 5535 bp open-reading frame (ORF) of 5535 bps without interruption (page 8, lines 30-32). The specification teaches that the ORF is preceded by a 490 bp intron (including a consensus splice acceptor) and 19 bps of 5'UTR. The response asserts that "the entire ORF may be coded for by a single exon (we are still missing the sequences coding for the last 12 amino acids (36 bp)) (page 9, lines 2-4).

The art teaches the genomic structure of RAI1 (Seranski et al. Gene, Vol. 270, No. 1-2, pages 69-76, 2001). The RAI1 gene for retinoid-acid induced protein 1

contains approximately 10200 nucleotides. Genbank Accession Number AJ271791 depicts the nucleic acid and provides the intron/exon structure of the nucleic acid. Exons 1-7 are depicted. The nucleic acid of RAI1 is 98% identical with SEQ ID NO: 5 over the entire length and a local similarity of 99.6% (see alignment). Therefore, provided that the RAI1 gene and the instant hGT1 gene are the same gene, it does not appear that at the time of filing applicant was in possession of either the full cDNA nor a gene with introns, and regulatory sequences.

Much like Example 6 and 7 in the Written Description Guidelines, the instant specification teaches a fragment of the coding sequence, namely SEQ ID NO: 5. The specification admits that the sequences coding for the last 12 amino acids are missing. Therefore, the coding sequence is a partial coding sequence. Therefore, claims directed to the human gene, for example, Claims 1, 15-16, have not been adequately described. There is no actual reduction to practice of the claimed invention, clear depiction of the claimed invention in the drawings or complete detailed description of the structure. There is a disclosure of the partial structure, namely SEQ ID NO: 7-12, however, there is no known or disclosed correlation between this function and structure of the non-described regulatory elements and the untranslated regions of the gene. The present claim encompasses full-length genes and cDNAs that are not further described. There is substantial variability among the species of DNAs encompassed within the scope of the claims because SEQ ID NO: 7-12 is only a fragment of any full-length gene or cDNA species. One skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of genes which comprise

SEQ ID NO: 5. Furthermore, the claims are directed to any gene comprising (CAR)2(CAG)nCAA wherein R is A or G and n is from 7-12. This is only a partial structure which does not clearly define the genus of genes which comprise the partial structure.

With respect to the claims directed to SEQ ID NO: 5, the claims lack description because SEQ ID NO: 5 is a partial cDNA also which is missing nucleotide bases as admitted in the specification. SEQ ID NO: 2 appears to contain 13CAG followed by CAA. This sequence is not the full cDNA, therefore, a claim directed to the gene or comprising has not been described. The regulatory regions, the introns (if any) and the untranslated regions have not been described.

Furthermore, it is unclear that SEQ ID NO: 5 is a coding sequence which codes for an amino acid sequence. As provided above, and in the response filed June 28, 2002, the translation of SEQ ID NO: 5 contains three stop codons in the middle of the SEQ ID NO: 5. Therefore, it is unclear that SEQ ID NO: 5 as written is a sequence which encodes a single amino acid sequence. With respect to Claim 19 which is directed to any nucleic acid sequence comprising a sequence encoding the amino acid sequence as set forth in SEQ ID NO: 6, the specification does not describe such sequences.

Response to Arguments

The response traverses the rejection. The response asserts that "at the time of filing the Applicant was in possession of a significant portion of the hGT1 encoded protein, and had determined that it comprised polymorphic regions which could be

linked to psychiatric disease." This argument has been reviewed but is not convincing because the description of a "significant portion" of a gene is not description for the gene. Furthermore, a gene is comprises of introns, exons, regulatory regions and downstream regions. The instant application fails to provide each of these regions. Moreover, the presence of a partial cDNA (i.e. missing the last 12 amino acids does not provide written description for a gene, as taught in the Written Description guidelines. Furthermore, taking the post filing date art, namely Seranski, the art teaches a nucleic acid with 99.8% similarity which comprises 7 exons. The instant specification does not teach introns or these exons. It is noted that the claims are drawn to a gene, not a polymorphic region of the nucleic acid. Therefore, a "gene" has not been described.

The response argues that the "coding potential of SEQ ID NO: 5" is clearly and distinctly enabled and described in the application as originally filed. This argument has been thoroughly reviewed, but is not found persuasive because the protein of SEQ ID NO: 6 is a partial protein which was not originally described in the instant application, as discussed above.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 9-11, 13-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for short CAG repeat allelic variants of hGT1 associated with schizophrenia, does not reasonably provide enablement for any allelic variants of hGT1 associated with any disorder such as psychiatric diseases, affective disorders, neurodevelopment brain disease and phenotypic variability with response to long term response to neuroleptic medication. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to an isolated human hGT1 gene comprising a transcribed polymorphic CAG repeat having the sequence (CAR)2(CAG)n(CAA) wherein R is A or G and n is from 7-12, wherein allelic variants of said CAG repeat are associated with a disorder and wherein n being equal to 11 is the most common allele of the hGT1 gene.

The specification describes a nucleic acid, SEQ ID NO: 5, which is 6022 nucleotides in length. The specification the GT1 sequence includes a 5535 bp open-reading frame (ORF) of 5535 bps without interruption (page 8, lines 30-32). The specification teaches that the ORF is preceded by a 490 bp intron (including a consensus splice acceptor) and 19 bps of 5'UTR. The response asserts that "the entire ORF may be coded for by a single exon (we are still missing the sequences coding for the last 12 amino acids (36 bp)) (page 9, lines 2-4). The specification teaches that short CAG repeat allelic variants of the hGT1 gene were associated with schizophrenia irrespective of neuroleptic response (p=0.005) (page 8, lines 17-19). The association

was shown to be highly significant in Rs (p=0.0009) and marginally in NRs (p=0.12) (page 8, lines 19-20). The specification classified the alleles into long and short alleles (page 17, lines 32-34). As seen in Table 3 (page 18), a summary of the analysis in the schizophrenic patients is provided. The specification teaches that the "longer the size, the worse and poorer is the outcome" (page 19, lines 24-26).

The art teaches the genomic structure of RAI1 (Seranski et al. Gene, Vol. 270, No. 1-2, pages 69-76, 2001). The RAI1 gene for retinoid-acid induced protein 1 contains approximately 10200 nucleotides. Genbank Accession Number AJ271791 depicts the nucleic acid and provides the intron/exon structure of the nucleic acid. Exons 1-7 are depicted. The nucleic acid of RAI1 is 98% identical with SEQ ID NO: 5 over the entire length and a local similarity of 99.6% (see attached alignment). Therefore, provided that the RAI1 gene and the instant hGT1 gene are the same gene, it does not appear that at the time of filing applicant was in possession of either the full cDNA nor a gene with introns, and regulatory sequences.

Moreover, the art teaches the length of the CAG repeat in the RAI1 gene modifies the age of onset of SCA2 (abstract)(Figueroa et al. Arch Neurol. Vol. 58, No. 10, pages 1649-1653, October 2001; Hayes et al. Hum. Mol. Genetics Vol. 9, No. 12, pages 1753-1758, 2000).

Based upon the specification, it is unclear how the short alleles and long alleles correspond to number of CAG repeats, to n=7-12 and to SEQ ID NO: 12-17. The specification teaches that PCR amplified fragments range from 171-183 nucleotides. The number of CAG repeats range from 11-15. And the specification has designated

these –3 to 1 (page 4). The specification teaches the most common allele is 180 bp or 14 CAG repeats is taken as 0. However based upon the claim language, SEQ ID NO: 16 is the most common allele with n=11 wherein n is the CAG repeats. Therefore, it is unclear whether the common allele has 11 or 14 CAG repeats. The analysis in the specification appear to group n=11 into the long alleles for analysis purposes. Therefore, it is unclear whether n=11 is a control or whether n=11 is also associated with schizophrenia. Based upon the specification and the claim 1, it appears as though n=11 was associated with severe schizophrenia. However based upon Claim 13, it does not appear that applicants are claiming an association between n=11 and schizophrenia. The specification does not appear to indicate that n=7 corresponds to either shorter or longer alleles. The specification appears to place n=11, the common allele within the analysis of longer alleles (page 5, lines 30-31). Applicant's may with to use SEQ ID NO:s rather than allele numbers or n= to ensure clarity.

Thus neither the specification nor the art teach the skilled artisan how to use the invention as broadly as claimed. The specification has not provided analysis of any psychiatric disease, affective disorders, neurodevelopmental brain diseases and phenotypic variability with respect to long term response to neuroleptic medication. The specification does not provide any analysis of the association of the instant nucleic acids with the listed disorders. The specification has not provided any analysis of affective disorders, including manic depression. The genus of diseases within psychiatric disease, affective disorders, neurodevelopmental brain diseases and phenotypic variability with respect to long term response to neuroleptic medication is a

very diverse set of diseases or disorders. Affective disorders are defined as a class of mental disorder's characterized by a disturbance in mood. The class of affective disorders includes manic depression, seasonal affective disorder, biopolar, for example. Each of these disorders is not well understood and does not appear to have a common pathway or mode of action. Therefore, absent guidance in the specification, it is not predictable that all affective disorders function in the same manner such that it would be expectable that association of a gene variant with a single disorder would be indicative of association with the whole class of disorders. Similarly, psychiatric disorders is a diverse class of diseases which includes for example, Psychotic Disorders (Schizophrenia and Other Psychotic Disorders), Mood Disorders (Depressive and Bipolar), Anxiety Disorders, Substance Abuse Disorders, Personality Disorders, Somatoform Disorders, Eating, Sleeping & Impulse Control Disorders. It is unpredictable as to whether any quantity of experimentation would allow one to practice the claimed invention.

Response to Arguments

The response traverses the rejection. The response asserts "in view of the teachings of the present invention, and for example the teachings at page 23....that claims 1-5, 9-11, 13-25 would be considered enabled by a person of ordinary skill in the art to which the present invention pertains." This argument has been reviewed but is not convincing because the response fails to provide any technical reasons why the specification, at page 23, overcomes the rejection of record. The citation that the response points to is merely a statement of further interest, and does not provide any

enabling support for the claims. The response fails to address the rejection to the extent that it applies to various broad classes of diseases. Therefore, since no amendments have been made and the arguments are not persuasive, for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-5, 9-11, 13-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-5, 9-11, 13-25 are indefinite because the designation hGT1 is arbitrary. The instantly disclosed nucleic acid could be identified by some other arbitrary name, such as rai1 or gsgti, or the name hGT1 could be arbitrarily used to designate another nucleic acid. This rejection may be overcome by providing descriptive characterization of the claimed polypeptide.

Response to Arguments

The response traverses the rejection. The response asserts that the claim has been amended to provide a descriptive characterization of the claimed polynucleotide. This argument has been reviewed but is not convincing because the claim remains unclear as to whether the human gene much comprising a nucleic acid encoding SEQ

ID NO: 6 or whether SEQ ID NO: 6 is merely the most common allele. Therefore, the claim remains unclear as to the structure of the gene aside from a glutamine repeat region. Thus for the reasons above and those already of record, the rejection is maintained.

B) Claims 1-5, 9-11, 13-25 are indefinite because it is unclear whether applicant is claiming a nucleic acid sequence which is normal or whether applicant is claiming variants of the normal which are associated with a disease. The claim requires a nucleic acid comprising a CAG repeat having the sequence provided wherein alleleic variants are associated with a disorder and wherein n being equal to 11 is the most common allele. It is unclear whether the claim is, therefore, limited n equal to 11. The metes and bounds of the claimed invention are unclear.

Response to Arguments

The response traverses the rejection. The response asserts the claim has been clarified. This argument has been reviewed but is not convincing because the claim amendments still contain reference to the allelic variants. It is unclear whether the claim is drawn only to allelic variants or whether the claim is also drawn to the normal common allele. Thus for the reasons above and those already of record, the rejection is maintained.

D) The term "less severe schizophrenia" in claim 3 is a relative term which renders the claim indefinite. The term "less severe" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one

of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification provides different categories of severity of schizophrenia, Figure 2, however, it is unclear which of these categories is deemed "less severe".

Response to Arguments

The response traverses the rejection. The response asserts that the recitation "less severe schizophrenia" is not indefinite based upon the teachings at page 21. This argument has been reviewed but is not convincing because the specification does not provide any standard for severe, less severe schizophrenia. It is unclear what the term encompasses. Thus for the reasons above and those already of record, the rejection is maintained.

E) Claims 4-5, 9 are indefinite over the recitation "are indicative of a neuroleptic response" because it is unclear based upon the claim and the specification what is encompassed by a neuroleptic response. It is unclear whether there is a positive response, no response, intermediate response, adverse response or another type of undisclosed response.

Response to Arguments

The response traverses the rejection. The response asserts that neuroleptic response is clearly defined as a response which improves symptoms of a patient. This argument has been reviewed but is not convincing because the words on page 1-2 do not provide an adequate definition for the terms. The specification merely talks about the potential of neuroleptic medication, not of a neuroleptic response or what constitutes such a response.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10. Claims 1-2, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Neri et al. (WO 97/30178, August 21, 1997).

It is noted that the intended use of the allelic variants for does not carry patentable weight in the product claim. It is noted that Neri teaches a human nucleic acid comprising CAG20CAA. Therefore, the structural limitations of the claim have been met and the product is anticipated.

Neri et al teaches transcribed DNA sequence with a high level of CAG repeat codons which are useful in diagnosing trinucleotide repeat diseases. SEQ ID NO: 19 of Neri teaches a nucleic acid from chromosome 3p14 which comprises (has) CAG20CAA (see page 22, line 2 of sequence listing). Therefore, Neri teaches an isolated nucleic acid having the sequence of SEQ ID NO: 12-17. Since Neri has taught all of the limitations of the claims, Neri anticipates the claimed invention.

Response to Arguments

The response traverses the rejection. The response asserts that "since n is defined as being from 7-12, the sequence of the present invention therefore are from CAG9CAA to CAG14CAA." The response further asserts that "Clearly, these sequences are not taught nor suggested by the CAG20CAA sequence of Neri." This argument has been reviewed but is not convincing because the claim is drawn to an isolated sequence comprising a transcribed polymorphic CAG repeat having the sequence CAR2CAGnCAA. Comprising is open claim language which allows additional sequences to be on either side of the nucleic acid. Therefore, Neri teaches a nucleic acid comprising each of CAG9CAA, CAG10CAA, CAG11CAA, CAG12CAA, CAG13CAA and CAG14CAA. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

11. No claims allowable.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
May 13, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

FORM PTO-1449 U.S. Department of Commerce Patent & Trademark Office	Attorney Docket No. 2055GG/48747TR	Serial No. 09/508,821
INFORMATION DISCLOSURE STATEMENT *(Use several sheets if necessary)*	Applicant: Guy A. ROULEAU, et al.	
	Filing Date May 26, 2000	Group

MAR 1 3 2003

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date (if appropriate)
	AA						
	AB						

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	TRANSLATION Yes	TRANSLATION No
GG	AC	95/01437	01/1995	WO				
	AD	97/18825	05/1997	WO				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

GG	AE	Y. IMAI, et al. "Cloning of a retinoic acid-induced gene, GT1 in the embryonal carcinoma cell line P19: neuron-specific expression in the mouse brain" Molecular Brain Research, see whole document
	AF	Y. ROBITAILLE, et al., "The neuropathology of CAG repeat diseases: review and update of genetic and molecular features" Brain Pathology, Vol. 7, No. 3, July 1997, pages 901-926
	AG	P. MACIEL, et al., "Correlation between CAG repeat length and clinical features in Machado-Joseph Disease" American Journal of Human Genetics, Vol. 57, No. 1, July 1995, pages 54-61
	AH	R. JOOBER, et al., "Apolipoprotein E gentype in Schizophrenia" American Journal of Medical Genetics (Neuropsychiatric Genetics), Vol. 67, No. 2, April 9, 1996, page 235
	AI	R. A. PHILBERT, et al., "The characterization and sequence analysis of thirty CTG-repeat containing genomic cosmid clones" European Journal of Human Genetics, Vol. 6, No. 1, January 1998, pages 89-94
	AJ	G. TURECKI, et al., "Schizophrenia and chromosome 6p" American Journal of Medical Genetics" Vol. 74, No. 2, 1997, pages 195-198
	AK	S. F. ALTSCHUL, et al., Journal of Molecular Biology, Vol. 215, 1990, pages 403-410
	AL	J. I. NURNBERGER, et al., Archives of General Psychiatry, Vol. 51, 1994, pages 849-859
	AM	M. G. WOERNER, et al., Psychopharmacology Bulletin, Vol. 24, 1988, pages 112-117

EXAMINER G Goldberg DATE CONSIDERED 5/12/03

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

APPLICANTS MAY SUBMIT AMENDMENTS TO SPECIFICATION, CLAIMS AND DRAWINGS IN THE REVISED AMENDMENT FORMAT

For amendments filed in Art Units 1626, 1634, 1731, 2827 and 2834

Starting in late April 2003, the United States Patent and Trademark Office (USPTO) will be processing patent applications in electronic image form in Art Units 1626 and 1731 in addition to the three original Art Units (1634, 2827 and 2834) in the "prototype program"[1]. Applicants with applications in these art units are encouraged to use a revised amendment format for amendments to the claims, specification, and drawings, announced in *AMENDMENTS IN A REVISED FORMAT NOW PERMITTED*, 1267 Off. Gazette 106 (February 25, 2003), posted on the Office's web site at: http://www.uspto.gov/web/offices/com/sol/og/2003/week08/patform.htm. A summary of the revised amendment format is reproduced below.

The revised amendment format is essentially the same as the amendment format that the Office is proposing in a revision to 37 CFR 1.121 (Manner of Making Amendments). The revision to 37 CFR 1.121 (if adopted) will simplify amendment submission and improve file management. The Office plans to adopt such a revision to 37 CFR 1.121 by July of 2003[2], at which point compliance with revised 37 CFR 1.121 will become mandatory.

Effective immediately, when replying to Office actions in applications from Art Units 1626, 1634, 1731, 2827 and 2834 **all** applicants are encouraged to submit amendments using the revised amendment format (except for reissues and reexaminations), and which will be processed according to conditions specified herein.

REVISED FORMAT OF AMENDMENTS

Begin on separate sheets:
Each section of an Amendment (e.g., Claim Amendments, Specification Amendments, Remarks) should begin on a separate sheet. *For example*, in an amendment containing a.) introductory comments, b.) amendments to the claims, c.) amendments to the specification, and d.) remarks, each of these sections should begin on a separate sheet. This will facilitate the process of separately indexing and scanning of each part of an amendment document for placement in an electronic file wrapper.

Two versions of amended part(s) no longer required:
The current requirement in 37 CFR 1.121(b) and (c) to provide two versions (a clean version and a marked up version) of each replacement paragraph, section, or claim will be waived where an amendment is submitted in the revised format below. The requirements for substitute specifications under 37 CFR 1.125 will be retained.

A) Amendments to the claims:
Each amendment document that includes a change to an existing claim, or submission of a new claim, must include a complete listing of all claims in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.

(1) The current status of all of the claims in the application, including any previously canceled or withdrawn claims, must be given. Status is indicated in a parenthetical expression following the claim number and identified by one of the following: (original), (currently amended), (previously amended), (canceled), (withdrawn), (new), (previously added), (reinstated – formerly claim #_), (previously reinstated), (re-presented – formerly dependent claim #_), or (previously re-presented). The text of all pending claims under examination must be submitted each time any claim is amended. Canceled and withdrawn claims should be indicated by only the claim number and status.

(2) All claims being currently amended must be presented with markings to indicate the changes that have been made relative to the immediate prior version. The changes in any amended claim should be shown by strikethrough (for

[1] See *USPTO ANNOUNCES PROTOTYPE OF IMAGE PROCESSING, 1265 Off. Gaz. Pat. Office 87* (December 17, 2002)). The amendment practice of the Notice only provided for a waiver of 37 CFR 1.121(c), with respect to amendments to the claims. This flyer supercedes any previously received notification and now encourages the presentation of amendments in an expanded format, which applies to the amendment of specifications, drawings and claims.

[2] See *Changes To Implement Electronic Maintenance of Official Patent Application Records*, 68 Fed. Reg. 14365, (March 25, 2003).

deleted matter) or underlining (for added matter). An accompanying clean version is not required and should not be presented. Only claims of the status "currently amended" will include markings.

(3) The text of pending claims not being amended must be presented in each amendment document in clean version, i.e., without any markings. Any claim presented in clean version will constitute an assertion that it has not been changed relative to the immediate prior version.

(4) A claim may be canceled by merely providing an instruction to cancel. Listing a claim as canceled will constitute an instruction to cancel. Any claims added by amendment must be indicated as (new) and shall not be underlined.

(5) All of the claims in each amendment paper must be presented in ascending numerical order. Consecutive canceled or withdrawn claims may be aggregated into one statement (e.g. Claims 1 – 5 (canceled)).

Example of Listing of Claims:

Claims 1-5 (canceled)

Claim 6 (withdrawn)

Claim 7 (previously amended): A bucket with a handle.

Claim 8 (currently amended): A bucket with a ~~green~~ blue handle.

Claim 9 (withdrawn)

Claim 10 (original): A bucket with a wooden handle.

Claim 11 (canceled)

Claim 12 (re-presented – formerly dependent claim 11): A black bucket with a wooden handle.

Claim 13 (previously added): A bucket having a circumferential upper lip.

Claim 14 (new): A bucket with plastic sides and bottom.

B) Amendments to the Specification:

Amendments to the specification must be made by presenting a replacement paragraph or section marked up to show changes made relative to the immediate prior version. An accompanying clean version is not required and should not be presented. If a substitute specification is being submitted to incorporate extensive amendments, both a clean version (which will be entered) and a marked up version must be submitted as per current 37 CFR 1.125.

C) Amendments to the drawings:

Drawing changes must be made by presenting replacement figures which incorporate the desired changes and which comply with § 1.84. An explanation of the changes made must be presented in the remarks section of the amendment. Any replacement drawing sheet must include all of the figures appearing on the immediate prior version of the sheet, even though only one figure may be amended. The figure or figure number of the amended drawing should **not** be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

COPIES OF U.S. PATENT DOCUMENTS CITED IN AN IDS OR OFFICE ACTION

In applications assigned to the five art units listed above, applicants and practitioners will no longer be required to provide copies of U.S. Patents and U.S. Patent Application Publications cited in any Information Disclosure Statement (IDS) submitted to the USPTO. It is requested that eIDSs be used to file all IDS papers for applications in the listed Art Units. Similarly, copies of U.S. Patents and U.S. Patent Application Publications cited by an examiner during prosecution of an application will not be provided to applicants in Office actions from these Art Units. These documents are available from the USPTO web site, www.uspto.gov , for free download. Cited foreign patents and published applications and non-patent literature will be mailed by conventional processing.

Any questions regarding the submission of amendments pursuant to the revised practice set forth in this flyer should be directed to Liz Dougherty (Elizabeth.Dougherty@uspto.gov), Eugenia Jones (Eugenia.Jones@uspto.gov) or Joe Narcavage (Joseph.Narcavage@uspto.gov). For information on the waiver or legal aspects of the program, please contact Jay Lucas (Jay.Lucas@uspto.gov) or Rob Clarke (Robert.Clarke@uspto.gov).

The United States Patent and Trademark Office has changed certain mailing addresses!

Effective May 1, 2003

Use the address **provided in this flyer after May 1, 2003** for **any correspondence** with the United States Patent and Trademark Office (USPTO) in patent-related matters **to organizations reporting to the Commissioner for Patents.**

DO NOT USE the Washington DC 20231 and P.O. Box 2327 Arlington, VA 22202 addresses after May 1, 2003 for **any correspondence** with the USPTO even if these old addresses are indicated in the accompanying Office action or Notice or in any other action, notice, material, form, instruction or *other* information.

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Also effective May 1, 2003, the **USPTO is changing the special Box designations for Patents and Trademarks to corresponding Mail Stop designations** (*e.g.*, "Box 4" will now be "Mail Stop 4").

For further information, see *Correspondence with the United States Patent and Trademark Office*, 68 *Fed. Reg. 14332* (March 25, 2003). A copy of the *Federal Register* notice is available on the USPTO's web site at http://www.uspto.gov/web/menu/current.html#register

A listing of specific USPTO mailing addresses (See Patents – specific) will be available on the USPTO's web site on April 15, 2003 at http://www.uspto.gov/main/contacts.htm

Persons filing correspondence with the Office should check the rules of practice, the Official Gazette, or the Office's Internet Web site (www.uspto.gov) to determine the appropriate address and Mail Stop Designation (if applicable) for all correspondence being delivered to the USPTO via the United States Postal Service (USPS).

Questions regarding the content of this flyer should be directed to the Inventor Assistance Center at (703) 308-4357 or toll-free at 1-800-786-9199.